IN THE DISTRICT COURT OF THE UNITED STATES
DISTRICT OF SOUTH CAROLINA
CHARLESTON DIVISION

TERRENCE SPARKMAN, et al,	)	2:12-CV-2957
	)	
Plaintiffs	)	Charleston,
	)	South Carolina
VS	)	August 17, 2015
	)	
GOULDS PUMPS, INC.,	)	
	)	
Defendant	)	

TRANSCRIPT OF TRIAL TESTIMONY OF DR. ARNOLD BRODY
BEFORE THE HONORABLE DAVID C. NORTON,
UNITED STATES DISTRICT JUDGE

APPEARANCES:

For the Plaintiff: MR. JOHN HERRICK
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Proceedings recorded by mechanical shorthand,
Transcript produced by computer-aided transcription.

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MR. HERRICK: Your Honor, our next witness will be Dr. Arnold Brody.

THE COURT: Okay.

THE CLERK: Please come forward to be sworn here at the Bible. Right here, sir.

Can you please place your left hand on the Bible and raise your right hand.

State your name.

THE WITNESS: Arnold R. Brody, B R O D Y.

THEREUPON:

DR. ARNOLD R. BRODY,

Called in these proceedings and after having been first duly sworn testifies as follows:

THE CLERK: You may have a seat in the witness stand.

THE WITNESS: Thank you.

DIRECT EXAMINATION

BY MR. HERRICK:

Q. Good afternoon, Dr. Brody.

A. Good afternoon.

Q. I told the jury in opening statement that you were the witness who was going to come in and testify about how asbestos gets in into the body and translocates through different parts. Are you, in fact, going to talk about that

today?

A. Certainly.

Q. Okay. Let's talk a little bit about your background, Dr. Brody.

Where are you from and what do you do?

A. So I'm a professor emeritus at the pathology department at Tulane University in the medical school in New Orleans. I was there for many years. I was the vice chairman at the pathology department at Tulane and I retired in 2011. And I was honored with the position of professor emeritus. Emeritus is from the Latin out of merit or from honor. And I continued to work with colleagues there. Even though I'm retired, I work with colleagues there. And we are carrying on our work in understanding how asbestos causes disease. And we are focused now on lung cancer, but we have been studying mesothelioma and mesothelial cells for many years.

Q. Doctor, are you a medical doctor?

A. No. I'm a Ph.D.

Q. Okay. Give us the benefit of your background, if you would --

A. Um-hum.

Q. -- and training.

A. Okay. So after high school in New Hampshire, I went out to Colorado to do a bachelor of science degree in zoology. Zoology is the study of animals. I then went to the

University of Illinois where I received a master of science degree in anatomy, that's animal anatomy, human anatomy. That's where we learn how all of our parts fit together and function: Muscles, bones, nerves, joints, that sort of thing. Then I went back to Colorado to do a Ph.D., that's the doctorate, and that's in cell biology.

Every living thing is made of cells. We need to understand how cells function. Every disease has a target cell from which that disease develops. And so I have been focusing on lung cells and the target cells for the various asbestos-induced diseases.

Then I did three years of post doctoral study at Ohio State University. And then I started my academic career.

Q. And what was your post-doc study at Ohio State related to?

A. Well, this was a great opportunity to study a little creature that causes house dust allergies. I mean, you've probably heard of people allergic to the dust in their homes, and it's typically because there are little mites that live in there. Mites, M I T E S. And these mites shed their skin and they leave debris around. And people develop allergies to these mites. And I got to study these and study the anatomy of the house dust mite and what they leave around that makes us allergic.

Q. That was some research you were doing at that point in time?

A. That's actually where I started doing research. The post-doctoral study is where you find out if you have the kind of temperament that it takes to work in a basic science laboratory where you learn if you are the -- it is the thing for you. I mean, you try to -- do you want to be at a university or not? That kind of thing.

Q. And, Doctor, you said after your stint at Ohio State that you went on to your academic career?

A. That's right.

Q. And what was your academic career?

A. Well, that started as an assistant professor, that's a beginning professor, in the pathology department.

So pathology is the study of disease. And every medical school has a pathology department. So I was an assistant professor as a beginning professor in the pathology department at the University of Vermont in Burlington, Vermont. And I was there as -- a professor there for six years.

Q. So as a pathology professor at the University of Vermont, were you actually teaching medical students?

A. I did. And that's throughout my career. You know, it's not at all unusual for Ph.D.s to be professors in medical schools. We teach the basic sciences to the medical

students like biochemistry, embryology, anatomy, the things they need to understand before they go into their medical science. So that's not at all unusual for Ph.D.s to be in medical schools.

Q. And you told us that you were six years as a professor at the University of Vermont. What did you do next?

A. I was offered a position at the National Institute of Environmental Health Sciences. This is one of the National Institutes of Health. You maybe have heard of the National Heart Lung and Blood Institute, National Cancer Institute, these are all components of the Federal Government that are focused on human health.

The National Institute of Environmental Health Science where I was is obviously focused on how agents in the environment affect human health. And I was the head of the lung pathology laboratory there for 15 years.

Q. And what did you do as -- was this a teaching position?

A. No, not primarily. It was a research position to carry out fundamental basic science research. My focus was on how asbestos causes disease. But I had teaching opportunities at nearby Duke University and the University of North Carolina and North Carolina State University, as well.

Q. And so the NIHAS is located in North Carolina?

A. That's right.

Q. And you said you did that for 15 years?

A. I did.
Q. And, Doctor, what did you then next do in your career?
A. In 1993 I was offered a position as a full professor in the medical school at Tulane. That's what I was telling you about where I spent a large part of my career. So we moved to New Orleans and I started a laboratory there, again funded by the National Institutes of Health, through this competitive process where professors across the country write proposals to the National Institutes of Health and about -- only about 10 to 15 percent of those actually get funded. So it's a very competitive environment. I compete with the great schools in South Carolina and California and Texas and New York and everywhere across the country.

Professors in medical schools try to be supported by the National Institutes of Health. And my work was supported without interruption by the National Institutes of Health throughout my career.

In 1999 I was promoted to vice chairman of the pathology department and we were there through 2005. Actually, 2005 is when Hurricane Katrina came through and kind of blew us to the East Coast. My wife had already accepted a position at North Carolina State University. And when Tulane was closed and New Orleans was closed, I went to the Department of Molecular and Biomedical Sciences at North Carolina State sort of as a refugee and I was listed on the

website as a refugee.

And then the dean of the school there saw my grant portfolio, the support that I had from the National Institutes of Health, and he offered me a position as a professor there. So that's where I finished the last five years of my career, at North Carolina State. I retired in 2011.

From there -- and then 2012, as I said, I was honored with the position of professor emeritus, and that's my current academic position.

Q. So what we should take from this is the deans at medical schools like to hire researchers that have a history of getting grants approved?

A. Even better than that, if they actually have the grants in their pocket, and, yes, approved, absolutely. That's exactly right.

Q. Okay. The grant process is that competitive?

A. Exactly.

Q. And did you have to -- were you competing for grants when you were at the National Institute of Environmental Health scientists or was that automatic as part of the Government?

A. Well, it was part of the Government, but you could not -- it was still a merit system.

So in other words, papers that you got published were judged. And as you moved through the system, you were

competing. I mean, we had a budget. I wasn't writing grant proposals, but we had a budget. And those who successfully were publishing their work and being recognized by their peers in the field moved up through the system. And I reached the highest level of GS-15 it was called at the time.

Q. And, Doctor, has there been a common theme to your -- to your work in the lung pathology labs over your career?

A. Sure.

Q. What has that been?

A. Well, that is to focus on what we need to know about the asbestos diseases. I mean, today there are no effective treatments for any of the asbestos-related diseases. So the National Institutes of Health supports laboratories, and not just mine, but other laboratories where we are trying to learn enough about the disease process to block it, to treat it, to develop an effective treatment.

For example, there is a disease called asbestosis. That's scar tissue in the lung from inhaling asbestos. Well, we developed a strain of mice that is protected from getting asbestosis because we learned that this particular gene that drives a factor called the tumor necrosis factor is a requirement for the development of asbestosis. So if you knock that out, you can protect the animals.

Now, that's actually the basis -- not based on my

experiments -- but that is the basis for very commonly used drugs, like Humira and other drugs that block inflammation in arthritis and other diseases like that, because this gene is a driving force in inflammation. And it turned out that we discovered that it's a driving force in this disease, asbestosis. And we published a whole series of papers on how to block that.

Q. And asbestos is not the only thing that causes lung inflammation?

A. No. Of course there are a number of things that do.

Q. And how does your -- how does your research affect other causes of lung inflammation?

A. Well, these are general principles. In other words, while we use asbestos in my laboratory as a model to produce inflammation and scarring and cancer, you could -- you could use other things, as well, and those applications that are broad for other kinds of diseases. But I mean, I started my career working with the asbestos models, and that's what I've studied, and that's been the focus of my work.

Q. How is it that you came to be interested in using asbestos as a model so you could study inflammatory response?

A. When I was an assistant professor at the University of Vermont, it was sort of an early Saturday morning and I got a phone call from the department chairman. And he said, We have Dr. Chris Wagner, W A G N E R -- I don't know if you've

heard about Dr. Wagner yet, so -- it looks like Wagner -- but he's from South Africa. He pronounces his name "Vagner".

So Dr. Chris Wagner had established in 1960 that asbestos causes mesothelioma, this cancer that I know you've heard about. And so he was very well-known in the field and he had gone on then to develop an animal model. And he showed that if you exposed rats to asbestos, they get all the diseases that people do: Asbestosis, lung cancer, mesothelioma.

And here he was, a visit to the department, and the department chairman asked me if I wanted to visit with him. And of course I jumped on my bicycle and ran down there. And sitting across the table from Dr. Wagner who, showing him my work that I was doing, using different kinds of microscopes and electron microscopes and studying human disease, asbestosis and other diseases. And he asked me if I would like to come and work with him in Wales in the United Kingdom. He had moved from South Africa to Wales. And he asked me if I would like to work with him. And of course this was a spectacular opportunity.

I took my young family and we went to Wales in the United Kingdom. And I worked with Dr. Wagner for several months. And he showed me how to use this model system, which I brought back to my laboratory as a young scientist, and essentially went into that field knowing that asbestos

causes asbestosis, lung cancer and mesothelioma. But when you asked what sounds like a simple question, Well, where does the asbestos go? We know it goes in the lung, but the lung is a very complex organ. Where does it go? You couldn't go to the library, couldn't go to the medical school and find out the answer to that question. It was nowhere to be found. So I started a series of experiments that allowed us to answer that question.

And then the next question is, Okay, it goes in the lung, then what? How do the fibers damage the various cells of the lung? How does it cause the damage that's required to produce asbestosis? How does it cause the genetic damage that is required for lung cancer and mesothelioma? These are the broad questions that we've answered by doing very specific experiments to answer those questions.

Q. Now, Doctor, you talked about Dr. Wagner who in 1960 wrote about the relationship between asbestos and mesothelioma --

A. That's right.

Q. -- and the relationship. When was the relationship between asbestos and asbestosis written about?

A. You are saying when? Was that your question?

Q. Yes. When?

A. So that was the early part of that century in the 1920s and '30s were the first cases that were described in the

medical literature. I mean, there was some older cases than that, but these were the first that were in the open medical literature that anybody could find if they looked. So that was asbestosis.

Q. And then lung cancer, Doctor?

A. Lung cancer was in the 1950s that relationship, that association between asbestos exposure and lung cancer became clear.

Q. And I guess what I'm getting at is tell us whether or not your work was to attempt to determine whether or not asbestos caused these diseases?

A. As I say, I mean, when I started my work, we knew that asbestos caused asbestosis, lung cancer, mesothelioma, pleural plaques and other diseases. The issue was: How does it do it and how do we develop effective treatments? And like so many diseases, they are so complex that it's taken through -- it's going to take into the future to get the answers. I mean, there are some cancers that can be treated effectively, but most cannot be because they are so complex.

Q. And so do I understand, then, your Ph.D. in cell biology -- so this research that you have done is being looking at what's going on on the cellular level?

A. Well, it's different levels. I mean, it started by looking at the lung, the whole lung, right? I mean, the

epidemiology is -- epidemiology is the study of populations and who gets sick in that population and what they get sick from. That's the -- that's the science called epidemiology.

So scientists start with epidemiology. In other words -- I'm not an epidemiologist, but I'm saying the epidemiologist tells us where the problems are in society. Who gets sick and from what? Well, the asbestos diseases were killing hundreds of thousands of people. So that's a problem.

So we started looking. Like Dr. Wagner, you start looking at the lungs of people. Well, what does it look like? What does the disease look like? How extensive it? And what can we -- what do we have to do to understand what causes it? What is the process? We know that asbestos causes it, but how does it do that?

So that's where my research is focused. First by looking at the human lung, recreating that disease in a -- in an animal model. And I have to prove to my peers that I'm, in fact, reproducing that disease. I can't just say that I am, I have to prove that this is a re-creation of the human disease in the animal model.

And then we go to the cells, the individual cells. And today it's what's called the molecular level. Genes and genetics. All of these asbestos diseases are driven -- asbestosis, lung cancer, mesothelioma -- are driven by our

genes. Some of it is inherited; most of it is the outside influence of asbestos on specific genes.

Q. And does your work have any application beyond asbestos exposure?

A. Any disease that is caused by an agent in the environment has some overlap with what we are learning about asbestos. Of course.

Q. Doctor, you talked about meeting with Dr. Wagner who discovered this relationship between asbestos and mesothelioma in 1960. What fiber type was Dr. Wagner studying?

A. Well, he was living and working in a hospital in a mining town, essentially. And this was a Crocidolite mine. It's the kind of asbestos called blue asbestos. It's called blue because when you look at the ore and the rock, the mineral gives it a blue tint. And that's the -- and so here he was working as a pathologist, a young pathologist in this hospital, and here are people coming in with this rare cancer called mesothelioma. And he determined that essentially every one of these people, whether they were minors or if they lived in the community, essentially every one of them had been working with this Crocidolite asbestos. And so he made that association.

Q. So that was the blue African asbestos?

A. That's right.

Q. All right. Doctor, we've talked about -- for how many years have you now been doing this research since you met with Dr. Wagner and went to Wales?

A. You are going to date me, right? So that was -- so I started at the University of Vermont in 1972; 1974 is when I got to work with Dr. Wagner.

Q. So you have been doing this work since 1974?

A. Yes. That's correct.

Q. And how is it that you share your research with your colleagues in your profession?

A. Um-hum. Well, what we do is we write papers called peer reviewed papers because they are reviewed by our peers. And then they are published in the open medical literature so that anybody can see what we do.

Q. And have you, in fact, published papers in the medical/scientific literature?

A. I sure have. Sure.

Q. On what variety of subjects?

A. Well, most of them -- I mean, I have 153 peer reviewed papers. And I have 55 book chapters and invited procedures for meetings and things like that. So all of the book chapters and proceedings deal with asbestos and lung disease; all of -- most of the 153 peer reviewed papers, probably 120 or so of them deal with asbestos disease: Asbestosis, lung cancer, mesothelioma. And those that do not, I published

several papers on viral diseases, lung diseases and asthma.

Q. So for instance, I'm looking at your 60th publication, which was called *Asbestos Content of Lung Tissue and Asbestos Associated Diseases* in the *British Journal of Industrial Medicine* in 1986.

A. Okay.

Q. That would be an example of a peer reviewed publication?

A. Sure. The *British Journal* is a very good journal, yes.

Q. And that's the reason I picked that one. Unlike a lot of these journals, somebody might have heard of the *British Journal of Industrial Medicine*?

A. That's true, they may.

Q. Or the magazine *Chest*?

A. Right.

Q. That's a magazine for who?

A. That's mostly for chest physicians, doctors who are interested in the latest updates in the basic science of lung disease. But I published a number of papers in the *American Journal of Pathology*, the *American Journal of Respiratory and Critical Care Medicine*. There are a broad series of science journals that I have published in.

Q. And in fact, the one that I picked out, your 60th publication, you're published with a Dr. Roggli and a Dr. Pratt?

A. Right.

Q. Okay. And we told the jury that Dr. Roggli is actually going to be a witness in this case via videotape.

A. Okay.

Q. So you are familiar with Dr. Roggli?

A. Of course. Of course. Dr. Roggli is a pathologist at Duke University. He and I published a number of papers together. Sure.

Q. And we also told the jury that Dr. Richard Kradin, Mass General, is going to come tomorrow. You know Dr. Kradin?

A. Sure I do. And he and I -- actually, he was editing a book and he asked me to write a chapter in a book.

Q. So you have published with him, as well?

A. I have. Yes.

Q. And you mentioned invited -- well, what did you say, is invited --

A. Well, um, so I have been asked to speak at a number of different universities around the country and around the world, actually. And many times the results of that conference are published. So they are not peer reviewed, but they are compiled into a review of a topic. And they would appear -- if I write that, it would appear in that section of my CV. Or if somebody was writing a book, like Dr. Kradin was publishing a book, I might be asked to write a chapter on asbestos or on some topic related to that. And I've done that a number of times. And those are not peer

reviewed, they are -- I pull together my peer reviewed work and set it up as a review. And that's what that section of my CV is.

Q. Give the jury kind of a flavor for who might ask Dr. Brody to come give a talk and --

A. Um-hum.

Q. -- in a proceeding and where those proceedings might be?

A. Um, so there are -- the couple of different situations where I might be asked to give a talk. The most common one would be like at a university. Like for example I have been asked by the Harvard School of Public Health a couple of times to come and give talks there. The University of Southern California, UCLA, schools in New York and Florida and Texas and many schools around the country have asked me to come and give a talk to the scientists and the medical students at that particular university.

I might also be asked to give a talk at a conference. For example, I was asked two years ago to give a talk in Australia. And we went to Australia and I gave a talk there. I was a visiting professor at the Medical College of Beijing in China and was out there for two weeks working with the medical students. Things like that. There are a number of pages of invited talks that I've -- that I've done. And I've lectured to the medical students on these topics for decades.

Q. And, Doctor, you've got a slide show you are going to show us later which kind of goes through your -- the results of what you've learned over the years in observing asbestos inhalation among animals and where the asbestos goes and how it affects cells.

A. Right. So these are slides that most of which I've taken with various kinds of microscopes. I use these slides to explain to the medical students what is happening. I have shown them to many juries before. I used some of these slides in China and Australia and everyplace else. Anyplace that I'm asked to give a talk, I use some of these slides. And there is a lot of overlap in the way I explain things. I use a different vocabulary for a jury than I would for the medical students. But other than that, the concepts are the same.

Q. And I was just going to ask you that: Because of the work that you've done and the results that you've shown, have you been asked by lawyers like me to come and teach juries about how asbestos gets into our bodies and causes disease?

A. Many times. And by companies, as well.

Q. And you've done that with me on prior occasions?

A. I have. Sure.

Q. And you've been asked to do that in different places around the country?

A. I have. In fact, your law firm -- I don't even know if

you know this -- but your law firm was the very first one to ask me to come into a courtroom. That was 1989. It was 15 years after I started my interest in asbestos disease.

Q. And when my firm has asked you to testify, it's always been about your research?

A. That's right.

Q. All right.

MR. HERRICK: Your Honor, may I approach?

THE COURT: Sure.

Q. Let me hand you, Doctor, what's been marked as Exhibit SCGP 132 --

A. Okay.

Q. -- and ask if you can identify that.

A. Yes. This is a report that has been compiled for these proceedings.

Q. Okay. And does that also have with it a copy of your curriculum vitae?

A. Yes, it does.

Q. And tell the -- I use the term "curriculum vitae". That's a fancy term for resume that you doctors like to use, right?

A. That's correct.

Q. That's basically what we have been talking about here is your qualifications, your educational background, the various positions that you've held, and a list of your publications?

A. That's right. It's all here.
Q. Now, you told us that -- that you retired in 2011 and went to emeritus status at Tulane Medical School?
A. That's right.
Q. Describe for us how does that work with respect to the lab and your publications?
A. Um-hum. So when I was there as the vice chairman, I hired a number of young people just starting their academic careers. Two of them -- well, several of them -- but two of them are still there that I work with. A number of people that I hired are still there, but two of them I work with very closely. And on my CV are their publications that I've coauthored with them. And we continue today to, as I said, continue that line of research.
So for example, there is the disease lung cancer. Now, lung cancer is not mesothelioma. Lung cancer has a different target cell that I'll show you. And lung cancer is caused, as we know, by cigarette smoking. But if somebody smokes cigarettes and they are exposed to asbestos, they are much more likely to get a lung cancer than they are from asbestos alone or cigarette smoke alone. In other words, you can't just add the risk -- both of those create a risk, asbestos lung and cigarette smoke lung, but you don't just add those risks; you multiply those risks.
So behind that is a mechanism. There is a

biological mechanism that we don't know. We have some hypotheses, we think we know what is going on, but we are trying to test that. And that's some of the work that's going on right now at Tulane with one of those collaborators.

And then another thing that we are studying at Tulane is an area called stem cells. Now, you have probably heard of stem cells. These are not embryonic stem cells. Every one of our tissues has a stem cell population from which that tissue developed.

So for example, your skin. You always have to make new skin. You are always losing skin. You always have to make new skin. We have stem cells that are underlying this top layer of skin and they are producing new skin cells. Now, those cells can actually become tumor cells. It's called -- these can be what are called cancer stem cells. And any kind of tumor, the stem cell can be a central part of that. And that's the same with lung cancer. And in fact, we published a paper showing the cancer stem cells in mesotheliomas.

Now, with my other colleague, we are following this up by exposing animals to asbestos and finding where those stem cells are multiplying and developing and how they become cancer cells.

So that's what I'm doing with my emeritus status, being able to continue that kind of work with my former and

present colleagues.

Q. All right.

MR. HERRICK: Your Honor, I would move Exhibit SCGP 132 into evidence at this time.

MR. MCDONALD: Does that include his report?

MR. HERRICK: It does include the report.

MR. MCDONALD: I think we are going to take the reports out. We'll make that housekeeping. Otherwise, it comes in.

THE COURT: Without objection.

(Thereupon, Plaintiff's Exhibit Number 132 was received in evidence.)

MR. HERRICK: And, Your Honor, at this point in time I would offer Dr. Brody as an expert in cell biology, and particularly, the cellular and molecular affects of asbestos exposure.

MR. MCDONALD: I agree that Dr. Brody is qualified.

THE COURT: Okay. So qualified.

MR. HERRICK: Your Honor, this would be a good point to break for lunch if the Court is so inclined. The balance of Dr. Brody's testimony is about 45 minutes.

THE COURT: You can go to lunch right now. Don't discuss the case among yourselves, don't let anyone discuss it with you. We'll start again at 2:00. Okay?

(Thereupon, the jury retired from the courtroom.)

THE COURT: Okay. I'm looking at this bifurcation stuff. The trigger mechanism is that the defense requests it.

MR. MCDONALD: Okay.

THE COURT: Okay? So are you requesting it?

MR. MCDONALD: I am requesting it.

THE COURT: I'm not so sure it applies, but if you are not going to request it, I don't have to worry about it.

MR. MCDONALD: I was concerned that maybe -- I didn't want to interrupt things, your charge and stuff like that, but -- I don't know if I let the horse out, but certainly I want to apply the caps. I mean, even if I can't bifurcate.

THE COURT: Well, this statute says the caps do not get revealed to the jury anyway.

MR. MCDONALD: Sure. But I just want to make sure we are heading that way.

THE COURT: Okay.

MR. MCDONALD: Because the diagnosis was in July of 2012, so --

THE COURT: So are you or are you not moving to bifurcate this trial, assuming that this statute is relevant? You can think about that over lunch.

MR. MCDONALD: Thank you, Judge. It makes it so complicated to bifurcate.

THE COURT: I agree with you. We are heading down the same path. I don't have any problem. There is going to be some questions, we've got to do some research on it. There is something in here about it controls the admission of evidence.

MR. MCDONALD: That's right.

THE COURT: And I would say that my Army is bigger than the South Carolina Army. So I don't think this will control the admission of evidence.

MR. MCDONALD: When you think about it, what's relevant for negligence, except for like financial information, it's pretty close.

THE COURT: So I'll just wait for y'all to make that decision. If we want to go down that road, we'll have to do some work. If we don't want to go down that road, then we'll just call it a bump in the road, all right?

MR. MCDONALD: Sure.

THE COURT: We'll see y'all at 2:00. Thanks.

(Thereupon, there was a lunch recess.)

THE COURT: Ready to go?

(Thereupon, the jury returned to the courtroom.)

THE COURT: Y'all can sit down whenever you want to. That's fine.

Mr. Herrick?

MR. HERRICK: Thank you, Your Honor.

Q. Good afternoon, Dr. Brody.

A. Good afternoon.

MR. HERRICK: Good afternoon, ladies and gentlemen.

Q. Before we broke for lunch, we were discussing your research work in the mechanisms of how asbestos causes disease and various diseases including inflammation, asbestosis or cancer. Can you tell the jury kind of how your laboratory is set up and what sort of things are going on in there?

A. Right. So we start in -- so a basic science laboratory is one where you are trying to answer questions where the answers are not available. I mean, that's what moves the field forward. And so you have to know what other scientists are doing. And then you kind of fill in the spots as you are trying to understand these very complex disease processes.

So for example, we start -- as I mentioned, we start with a human disease by looking at the lungs of people, but then in my laboratory we have three layers of inquiry.

One is using the animal model. Now, think about any human disease. Just about every human disease has in the animal model, like tuberculosis, HIV, a number of different cancers, scientists have been able to produce a model system that allows you to understand the human disease.

I'll give you a good example. The disease

tuberculosis, which was called consumption, and killed millions of people through the Millenia, through the centuries. Earlier in this century and in the last century -- I'm sorry -- in the 1940s and '50s some scientists decide -- found out that the same bacteria, microbacteria that causes bacteria in people causes the same disease in mice. So now all of a sudden there was a way to start testing antibiotics, treat -- give the animals the disease that people get, treat them with antibiotics and see which ones work.

Decades later, they found a couple of very powerful and very effective antibiotics that are used today because of that animal model that they were able to develop. They are now -- we've found that there are some resistant strains of tuberculosis, and they are very difficult to treat, but the concept hasn't changed.

Now we are using the asbestos model to answer certain questions. And as we go through the slides I'll explain what questions we are actually asking. So that's the animal model.

Then the next point is to study the actual cells from which the disease develops. So for example, asbestosis is scar tissue in the lung from inhaling asbestos. Well, what cell makes scar tissue? If you cut your skin and you get a scar where you cut it, that's because there is a

particular cell there called a fibroblast. A fibroblast makes connective tissue wherever you need it in your body. So if you take your skin and you pinch it and let it go, it will pop back because we have this connective tissue that holds us all together, all made in just the right amount by this cell called a fibroblast. Now, when you injure the surrounding tissue, the fibroblast starts making more of this connective tissue and you get a scar.

Now, in your skin you don't think much about it, but if asbestos is injuring the lung and the fibroblast starts to grow, you get scar tissue in your lung, you get short of breath, you can't take a deep breath. So we've done a whole series of studies on the fibroblast, understanding what makes that cell grow and make connective tissue. So that's an example. There are a whole series of other kinds of cells we've studied in the lung.

Q. Doctor, so what type of a, for lack of a better term, of equipment do you use to look at the fibroblast?

A. So you need to -- the cell is way below what you can see with the naked eye. We need to use different kinds of microscopes, particularly electron microscopes. We use light microscopes, as well.

And then finally -- I'll just complete this thought -- finally, we go to the genetic level -- I think I mentioned this earlier -- which genes are driving the

disease?

So take the fibroblast again for a minute. There is a particular gene that codes for this connective tissue. Well, this fibroblast, that gene gets turned on and starts to make the connective tissue. By the same token, I'm going to explain to you that cancer develops when there are errors in genes that control cell growth. Cancer is the loss of control of cell growth. So we are studying in the laboratory at the genetic level what causes -- how asbestos causes errors, mistakes in those genes that control cell growth. So those are the kinds of things that are going on in my laboratory.

Q. Doctor, while you are talking about genes, what's the difference between a gene and a genome?

A. Well, the genome is the entire universe of the genes that make us what we are. There is actually a Human Genome Institute now. So I told you about the National Cancer Institute, Heart Lung and Blood Institute, I was at the Institute of Environmental Health Scientists, there is actually a National Human Genome Institute. It's the most recent -- it's the 25th of the 25 institutes. Because in that institute we are trying to understand what all of our genes do.

Humans have about 20,000 or so genes that make us what we are. Well, what do they do? What do they all do?

We know what about 80 percent of them do because of this Human Genome Institute. And the genes are the individual actors that make us what we are.

Q. And are they -- is this institute these -- you know, if we -- we've heard of the Human Genome Project. Who is doing that?

A. Those are scientists at the institute and also from grants that are provided that are won -- W O N -- that are won by the great universities across the country to study the human genome.

Q. All right. Now, Doctor, have you prepared a PowerPoint presentation which kind of takes us through the inhalation of asbestos and its affect on the body?

A. Yes.

MR. HERRICK: Your Honor, with your permission, I'll ask the Doctor to go ahead.

THE COURT: Sure.

MR. HERRICK: There we go. Thank you.

Q. Now, what do we have here, Doctor?

THE WITNESS: Can I stand?

THE COURT: Yeah.

THE WITNESS: Thank you, Your Honor.

THE COURT: If you go down, if you can keep your voice up so Amy can hear you.

THE WITNESS: I think I'll stand right here. Would

that be okay?

THE COURT: No problem.

THE WITNESS: And then I can talk to the jury and I can point at the screen.

Q. This appears to be a diagram of what, Doctor?

A. Right. So this is obviously a diagram I have taken from a textbook. And I know you know where your lungs are, but I just want to remind you that when you take a breath, the air comes through this tube called the trachea, or the windpipe. You can feel the top of your windpipe in the Adam's apple. The breath goes down a series of tubes called conducting airways, because they conduct air down into the lungs. And then you can see in among the tubes there is a lot of space, and that's where we exchange oxygen and carbon dioxide. I'll show you what that looks like in a second.

And then this black line that runs around the outside of the lung, that represents the pleura, P L E U R A. The pleura is a very thin -- I mean saran wrap thin -- membrane that wraps around the outside of the lungs, makes the lungs airtight like balloons.

There is a single cell layer around the outside of the lung and those are called mesothelial cells. So if somebody has a cancer of the mesothelial cells, it's called mesothelioma.

Now, I can -- I sort of used this diagram as a map

to show you where the different asbestos diseases develop. Lung cancer develops in the walls of these tubes. Asbestosis develops out in the gas exchange area. And then as I indicated, mesothelioma develops on the surface of the pleura. It also can develop on the inside surface of the rib cage because there is a mesothelial surface there, as well. And every time you breathe, your lungs rub up and down against the inside of your rib cage, but you don't feel that. You are not supposed to feel that because the mesothelial cells are making a fluid that produces the friction between the two layers. And that's the function of the mesothelial cell, so you don't feel it when you breathe.

And that's why when somebody starts developing a mesothelioma, it can be very painful because you are not -- the lungs aren't moving correctly, okay?

So I use diagrams a lot, and diagrams are very helpful. But it also -- and in many cases we have to use different kinds of microscopes. We have to use sometimes an electron microscope. And this is what the electron microscope looks like that I had in my laboratory. This microscope actually was a victim of Hurricane Katrina. I had this for many years. Very expensive, hundreds of thousands of dollars. They last a long time.

And I can take a piece of tissue as small as a period at the end of a sentence or as big as this device I

have in my hand and put that tissue into this door right here in front of me. And I see the -- I'm not sure -- you can see the way the picture should look. By looking over here on this screen over here, you can see how bright and the colors. But over here I guess it's washed out by the lights.

But anyway, so we enter the tissue into this door. And at the top of the column there is an electron gun and the column has been evacuated. So there is a vacuum in the column. We generate the electrons at the top of the column. They come through the vacuum and strike the sample that I put in the microscope. So the electrons then pass over the surface of the tissue, and at the ultramicroscopic level recreate what that material looks like. That tissue that I put in there, the details are recreated by the electrons. Then I can collect the electrons with these electronics. And in front of me appears on this screen is an image of whatever it is I'm looking at, which I can magnify hundreds of thousands of times. And then just off of the screen is a camera. So I can take a permanent image of whatever it is I'm looking at.

Q. Is that all one piece of equipment, Doctor?

A. Yes. That's right. The column and the electronics and the screen and -- yeah, all these switches and things down here are to magnify and enhance the image and lights and darks and contrasts and things like that.

Q. So is that an indirect way of looking at a specimen?

A. Well, it is in a sense because the electrons are actually forming the image. And then you collect the electrons and produce that, yes. So they are called -- right -- and they are called secondary electrons.

Q. And how long have electron microscopes been around?

A. Let's see. The first ones were available commercially in the 1950s, '60s. Then this -- and that was before this generation -- because I'm going to show you, you get a three-dimensional perspective with this kind of microscope. That three-dimensional perspective was not available until the '70s, or middle to late '70s.

Q. And for how long, Doctor, have you been working with electron microscopes?

A. Actually, my Ph.D. started using -- and that was in -- I don't know, gosh, let's see -- that was in 1968, '69 I started using some of the very first commercially available electron microscopes. So since then.

And the next picture I'm going to take a piece of the lung out and you are going to see the pleura running over the lung and you are going to see the conducting airways going up into the lung. So I'm going to cut this out. I put it into the door into the microscope and I take a picture of it. And it looks like this.

And you can see that the lung is made up of hundreds

of thousands -- hundreds of millions of small air spaces. You can see some of those conducting airways going up into the lung. And you can see the pleura. You see how thin the pleura is when I cut across the face of the lung. And the mesothelial cells sit out here on the surface of the pleura.

Q. So when people say our lungs look like a sponge, this is what they are talking about?

A. Exactly. Of course it's a sponge for air rather than water.

So what is happening is -- so the air -- the room air has about 20 percent oxygen. So you take a breath and the air fills these millions of air spaces. And I'm going to show you in a minute that running through the walls of these air spaces is the blood. All the blood in our bodies has to run through our lungs. And it picks up the 20 percent oxygen and sends it to our brain and our fingertips and our toes and our muscles. And you use up that oxygen and you produce carbon dioxide and it comes back to your lungs and you exhale. And that's going on all the time in our lungs. And that's the function of our lungs, to respire.

Now, I also should tell you that if a rat or a mouse went running by you right here would be doing exactly what you are doing, inhaling and exhaling the room air using exactly these same structures, extracting the 20 percent

oxygen, doing just what we are doing. And since they are using the same cells and they get the same diseases as we do, we can use them as these -- this model system as I described.

Now, we have -- humans and animals and rats and mice and all other air breathing animals have a series of defense mechanisms that protect us. So that --

Q. What are those?

A. Okay. So that means that as we walk around the street, outside here or anywhere else where there are in the environment a lot of different things that could make us sick: Bacteria, viruses, pollen grains, a few asbestos fibers, these are things that are always in the environment yet they don't make us sick. Typically they don't. And they don't because we have very good defense mechanisms that protect us. Our nose hairs, the very first defense mechanism, captures a lot of things. The moisture, the mucus and the moisture in the back of our throats. Very effective in trapping a lot of things that we inhale. But a lot of those things go right past that, those defenses, and land down in our airways. So in our airways we also have very effective defense mechanisms, and I'm going to show you what that looks like.

So I'm going to fill the screen with what's in that red spot. Now, it could be anywhere along the air space, airway surfaces, but I'm going to pick any spot here and I'm

going to fill the screen. I'm going to take a picture. And this is what the surface of our airways looks like. You can see if they are lined with these little hairlike structures down here, and they are not hairs at all, they are extensions of the cell surface called cilia. C I L I A. And they are constantly beating in a wave-like fashion. So that if something lands on our cilia, gets swept up to our mouth and we swallow it or spit it out.

Q. Doctor, this has a key down there, or a little marker down there. What is that?

A. Right. So this is a size marker, because we always want to know how big and small these things are. Particularly asbestos fibers, we want to know if they are big fibers, small fibers. And so we can use the size marker to know.

For example, this is 10 microns. That's the Greek sign for micron or micrometer. So it's easy to see 10 microns. It's easy to see 10 microns because I magnified this tens of thousands of times. The question is how big is a micron?

Q. How big is a micron?

A. You take your thumb and your forefinger and you make a little space you can just barely see with your naked eye -- naked eye, meaning no microscope, no magnifying glasses, just what you can see -- that's about a millimeter. So the human eye can resolve just about a millimeter.

Now take that millimeter and divide it a thousand times. So what you've done is you've made a thousand microns. Now obviously you can't -- you can just barely see a thousand microns, you can't see a hundred, you obviously can't see ten, but with the electron microscope it's easy to see 10 microns. If you want to know how long the cilia are, you just stand that bar up with your mind's eye and you will see that they are about 10 microns long.

Now, also notice that there is some cells here that don't have cilia, they are kind of naked, and those cells make mucus. And you don't think much about mucus unless you smoke cigarettes or you have a cold and you can feel that mucus being brought up to your mouth or you cough it up and you swallow it or spit it out. And that's an important function of the airway is to make mucus. And that's one of the ways we clear things out of the airways. And this combination of mucus and cilia we call the mucociliary escalator because it escalates things up to our mouth where we can swallow it and spit it out. And this is working all the time.

Q. Now, Doctor, you mentioned that there are different target cells for different types of lung cancer. And I think what you said was that lung cancer occurs in conducting airways?

A. Yeah. You are looking at the target cell for lung

cancer.

Q. Which -- we've got two different types of cells there?

A. Right. So the cell that makes mucus and the cell that becomes mucus cells, the stem cell that becomes mucus cell -- and the mucus cells are the -- are the target cells for lung cancer. So as a person inhales cigarette smoke day after day after day, the carcinogens cause genetic damage in these cells and eventually can become cancer cells. I'll explain how that happens in a few minutes.

Q. Okay.

A. Okay. So let's go back now out to the end of the airway and out into the gas exchange, because I want to show you that asbestos fibers land out here, but we have to get the asbestos fibers to the target cell for mesothelioma, and that's out in the surface of the lung. So I'm going to show you this for just a minute and talk about these air spaces.

So let's go past the escalator and out to the -- I'm sorry -- and out to the end of the airway where it opens out into the gas exchange. And you can see a few of the air spaces that we have in our lungs. It's a little hard to see. If you can see this one closely, you can see little holes in the walls where the blood runs.

Now, each of these air spaces fills with the room air or whatever air we are breathing and whatever particulates are in that air, some of them get caught in the

nose, some in the back of the throat, some go right down and land on the floor of the air spaces. So when we talk about -- when I talk about these air spaces, I think it's helpful if you think about this room that we are in as an air space. And you take the ceiling off and think of this air space we are all sitting in now, and if you look down on the floor I see -- I think I see some good carpet squares. If you think of each carpet square as a cell, then you have a concept of what the cells look like that cover all of our air spaces. Big, flat cells go up over the wall into the next air space and cover with a complete carpet all of our air spaces.

Now, it turns out that that is a pathway for the asbestos to get out to the pleura. And I'm going to show you how that happens, but I want to show you what that looks like first because I'm going to take us into a single human air space. So it could be any one of these air spaces. And I'm going to put the microscope -- you take the ceiling off, right? And I hang over the top of the room and we are going to focus right down on the carpet. So here we are now in a single human air space. And I'm outlining for you one of the carpet cells, but nature doesn't make squares very well; nature makes smooth, rounded surfaces. So that's a carpet oval, I guess you could say, rather than a carpet square, but the concept is the same. And it's next very tightly

enclosed. This is the ridge between this cell and this cell. And you can see how these -- there are these big, flat cells that make up the carpet.

Q. Now, obviously this is a higher magnification than what we were just looking at?

A. That's right. We were looking at these individual spaces. But now if you want to actually see what the carpet looks like, I focus in, I focus in on a single air space and now we can see them.

So there are these big, flat cells, and then there are these smaller cells with the bumps all over them. And these are two different kinds of cells that line all of our air spaces. And I'm going to give you the big word for these cells. These are epithelial cells. And epithelial cells cover surfaces. Your skin is an epithelium. We call it epidermis.

Now, these epithelial cells are of two types: There is this big, flat epithelial surface, and then there is the smaller cells with the bumps all over them. So that if the big, flat cells get injured by infection, by asbestos, by whatever the case may be, these smaller cells start to divide and take their place.

We -- every one of our air spaces has a repair mechanism because there are a lot of ways for lungs to get injured. And we know that asbestos is one of them. We've

published a whole series of papers on how these cells respond to asbestos. And when I say "our lungs," I'm talking about you and me and rats and cats and guinea pigs and dogs and giraffes and elephants. Everything that inhales air has these exact same cells and structures.

Q. We talked about on this slide the flat carpet cells.

A. Right.

Q. And then the fluffy cells.

A. Right.

Q. Are those two different type of cells?

A. They are both epithelial cells. And it's not often that you have such an easy descriptor that separates them. But the type -- but the big, flat cells are type 1 epithelial cells and the other ones are type 2 epithelial cells. So that's just the way that we differentiate between the two. And if the type 1 cells are damaged, the type 2 cells grow and flatten out and take their place.

Q. So the type 2 cells become type 1 cells?

A. Exactly. It's called -- the process is called differentiation. From one cell type to another.

Q. And that's something that has been studied and we know about, at least you know about?

A. We even knew that when I was a youngster. This is something we've known about the lung for a long time. Now, we didn't know that asbestos caused damage to these type lung

cells until I started my work, and then we wrote the paper that described that.

Okay. So we have one more line of defense. So I'm going to take us down -- even further down on to a human air space. I'm going to show you our last line of defense and then we'll talk about asbestos. So I'm going to focus the microscope right down here on the carpet. Remember the cell with the bumps all over it? Focus right here. And now there is the cell with the bumps. And if you want to see how pretty it can actually be, you can look over here on this screen and see the really nice definition of these cells.

So here is the carpet, the type 1 epithelium down here. Here is the type 2 epithelium. And then there are two actors -- two other actors here. There is this one kind of ruffled, not going anywhere, then there is this cell that is kind of stretched out. And this has a tail end and a couple of what are called false feet out in front of it. And I caught this cell in the act after it was going after this pollen grain right here.

This lung once belonged to somebody who was killed in a motorcycle accident. I was on the medical examiner's autopsy call and I went in and prepared this person's lung within a couple of hours of death. And I -- as I went from air space to air space with the microscope looking for interesting things to show the medical students, I saw these

two cells sitting on the air space surface on the carpet.

Now, we have these cells called macrophages, macro means big and phage means eater. They control our air space surfaces. They pick up things that don't belong there. When this guy was riding along on this motorcycle, I'm sure he was inhaling a lot of different things. One thing we know he inhaled was this pollen grain right here. And it zipped right past the escalator, right past the cilia and landed on the carpet.

We don't want any kind of foreign particles sitting on the epithelial carpet of the lungs. And these cells have very sensitive chemical detectors that allow them to find foreign particles. And this one was on the way to pick up this pollen grain. It was going to take the pollen grain into the substance of the cell; digest it; break it down. Not digest it for nutritional purposes, but to break it down. And then the cell crawls up onto the escalator. Every time you swallow, you swallow a few of your friends, these macrophages. They are constantly clearing our air space surfaces of things that don't belong there.

And we keep making new macrophages in our bone marrow. When the bone marrow cells reach the lung, they come out and settle in the lung and they do that in the liver and the brain and all parts of the body. We have these macrophages that keep things clean. They are particularly

important for finding bacteria and infectious agents, agents that typically don't make us sick because we have this very important defense mechanism.

Now I'm going to show you that these cells recognize the presence of asbestos. We discovered the chemical signal through which they find the asbestos fibers in the lung. But it turns out that the asbestos fibers are toxic, and they kill the macrophages, or many of them, and the macrophages become part of the disease process.

So here is where our defense mechanisms do what they are supposed to do and actually get killed by the agent that's inhaled and become part of the disease. And that's the case with a lot of things with the immune system, the immune cells respond, get damaged by the agent thereafter and it becomes a disease process.

Q. Now, Doctor, these macrophages, are those -- is that a single cell?

A. Yeah. So this is one cell that hadn't recognized a foreign agent. So it's not stretched out and going after anything right now. So it's stationary while this is another cell that was on the move when I fixed it, so to speak. And "fix" means -- has a real meaning because it means I used a chemical agent that stops all the lifelike activity and so it remains in a lifelike condition, but not going to change now. It's fixed. And all of us have about one to three

macrophages in every one of our air spaces if you don't smoke. If you smoke, you have hundreds because they are always trying to clean up the mess. But they're, as I say, an essential part of our defense mechanism.

Q. And the macrophages, those cells, they are not attached?

A. They are attached, but by a biological glue, okay? In other words, they can control how attached they are. By releasing -- you can see right here. And here is the tail end of the cell and it is attached to the epithelium. And here you can see it's not as attached.

But so there are points along the cell that are attached to the substrate, meaning whatever is underneath it. So we can take these cells out and put them in a dish, a plastic dish or a glass dish and give them the right kinds of nutrients, and they will move along in the glass dish. And we can feed them asbestos or whatever bacteria, whatever we want to, to study the biology of these cells.

Q. And when one of these -- say for instance this fellow on the motorcycle kept going and the macrophage grabs the pollen grain and then gets on the mucociliary escalator and gets either coughed out or swallowed, how does another macrophage get into that air space?

A. The blood is going into the walls. So if I took a big saw and I cut up this room and I held the cut surface, you would see the carpet, the floorboards, and then you would see

the interstitial space of the building. The interstitial space is the word commonly used for the spaces between the floors and the walls, from one room to the next. So what's in the space? Plumbing, contract, you know, building materials, whatever you need to keep it together. Do the same thing in the lung. Cut through the air space in the lung, hold up the cut surface, as I have many times, and what do you see? You see blood, blood vessels going through there, connective tissue, nerves, things that are required to -- for life, okay?

And so you take a breath and the air -- the oxygen diffuses through the carpet and into the blood. And if there are -- if you don't have the two or three macrophages that you need in every air space, there is a chemical signal, a chemical balance, so that any macrophages -- new macrophages made in the bone marrow, when they get to the lung, they detect it and they come out. They migrate from the blood flowing underneath up through the carpet and plant themselves right on the air space surface. It is amazing, I agree.

Q. All right. Now, Doctor, I think we were going to talk about now how asbestos works in this scenario with the different defense mechanisms that we've gone through.

A. Exactly. We've seen all the defense mechanisms and all the cells we need to see to understand what happens in the lung so we can talk about asbestos. Now, have you heard

about the different kinds of asbestos?

Q. They heard me talk about it in opening. But as the Judge said, what I say is not evidence. So why don't you tell us about the different types of asbestos.

A. Okay. So there are three commercially useful asbestos varieties that make up about 100 percent or 99.5 percent of all the asbestos use in the world. The kind most used, 95 percent of the asbestos used in the world, is this type called Chrysotile. And that's how it's spelled right here. And Chrysotile is -- was mined in many places around the world. It is still mined in Canada, Russia. And it is, as I say, the kind that's been used most. It's the kind that I use in my laboratory most. It -- what do I want to say about it? Okay. I'll come back to that.

Let me tell you about the other two types while I'm thinking about that. So 95 percent of the world uses Chrysotile. And then the other 5 percent are from a mineral group called amphibole, A M P H I B O L E. The amphibole minerals have two commercially useful asbestos varieties: One is Crocidolite, C R O C I D O L I T E. That's Crocidolite. The other is Amosite, A M O S I T E.

Now, there are other kinds of amphibole asbestos. The other two make up about the 5 percent that Chrysotile doesn't make up for the commercially useful.

I remembered what I wanted to tell you now.

Chrysotile asbestos is in a mineral group called serpentine. Serpentine is the actual mineral that it comes from. And the reason it's called serpentine is you see how some of these fibers are kind of curly and serpentlike. And when you look at the other -- and all the asbestos varieties are naturally occurring minerals that get mined out of the soil.

So this Chrysotile asbestos, when you look at it in the earth, in the soil, some of it is kind of wavy in the rock of the mineral, and like a serpent. So that's why it's called serpentine. It's actually the state rock in the State of California, okay? So -- and from that comes this commercially useful Chrysotile, which was 95 percent of the world's use.

Now, the other types, as I said, Crocidolite and Amosite, amphiboles, I've used those in my laboratory. I've used all three for all the experiments I'm going to tell you about. Inhalation to the toxicity experiments. I've used all of the different asbestos varieties. But I typically use Chrysotile because that's the type that was used most in the world.

Q. And, Doctor, the Crocidolite we talked about, that was the fiber that Dr. Wagner linked with what?

A. With mesothelioma.

So sometimes useful to talk about different colors because sometimes easier to remember. So when you look at

the Chrysotile asbestos, it has kind of a white or ashy appearance, so it's called white asbestos. The Amosite looks like brownish, called brown asbestos. The Crocidolite has a very clear blue tint to it because of the mineral structure, and that's called blue asbestos. That's the kind Dr. Wagner made that -- established association with.

Q. And you said you primarily used Chrysotile in your experiments?

A. Right. Dr. Wagner showed that all of the asbestos varieties cause asbestosis, lung cancer and mesothelioma in those experimental animals. So actually when I started my work, again, I didn't need to produce mesotheliomas in the animal model. And it's -- fortunately that's true because it takes a long time. You have to expose the animals through their life span, which is about two to three years. And then just like in people, a very few of them get the cancer at the end of their life span. So we knew that. That's already been published. So I stayed at the beginning of the disease. What happens when the asbestos gets into the system? How does it cause the injury and the damage to the DNA? How does it do that that we know leads to the cancer?

Q. Doctor, let me ask you -- stop you there. When you are talking about how long it takes to experimentally cause a mesothelioma in one of these animals, how does that fit in

with the concept of latency?

A. Yeah. So not very well. Because there is -- there are certain things you cannot do with animals, and that's one of them. You are not going to learn much about the -- how much time it takes for the tumor to develop in a human and you are not going to learn how much asbestos it takes, how much exposure it actually takes to cause a disease in humans by using animals. You can't do that. And I wouldn't try. And anybody who tries would be fooling themselves. But what is going on during the latency? If you are asking me that, I can tell you. We can use the animals to explain.

Q. Answer my stupid question first, which is: Why can't you determine the latency with the animals?

A. Well, they are very short-lived. They are only two to three years. And the latency of -- for people is more typically 40 to 50 years. And it can be anywhere between 20 and 80 years. But most of the cases cluster between 30 and 50 years.

Q. Is that true for all the different types of diseases caused by asbestos?

A. It is, yeah. They have long latencies for different reasons. The asbestosis -- we can go into that if you want -- but I mean, the latency, it's a very different disease. It's not a cancer, but yet it takes decades for the disease to be manifested in the clinic. We'll talk

about why that happens with cancer.

Q. What you are using is the Chrysotile to stimulate the response so you can look and see what's going on during this time that the asbestos is causing an effect on cells?

A. Chrysotile, Crocidolite, Amosite, whatever asbestos we are using, they are pretty much the same mechanisms. They are somewhat different mineralogically, but the way they cause disease is very much the same.

Q. How do you use asbestos in your laboratory to study disease?

A. A couple of different ways. One is by taking -- well, let's look at this asbestos first and then I'll answer that. That was a good question. I'll answer that.

And so you can see that there is a 1 micron bar right here. You can't see it very well, but there is a 1 micron bar. So you can see 1 micron because I magnified this, this says 4,300 times. So I magnified this high enough so you can see a micron pretty easily.

And now if you put the micron bar up against these fibers, you can see that some of them are hundreds of microns long as they go off the screen. Some of them are you can see start out as a micron and fracture down to half a micron or less. Some of them are curly; some of them are straight. And that's the point about asbestos, it's constantly breaking down and producing shorter and thinner fibers. And all the

fiber types do that. Chrysotile does it more than the others, but they are always breaking down.

Now, we made aerosols of this asbestos. So one of the ways that we studied it is with the animal model, and I'm going to show you that in a second. That's one of the things that we did. That's producing disease in the animals by having them inhale asbestos in special chambers.

The other thing we do is to take cells out of animals or out of people, put the cells in a dish. And as I say, with the right nutrients, those cells will divide and multiply and stay alive, and you can actually add the agents you are interested in studying, and you can watch the events happen and study them chemically and biochemically.

And then finally, we look at the interactions between the asbestos and the actual genes and the genetics, which genes are being affected and how by the asbestos fibers.

Q. And have you done all these experiments?

A. Yes. Right. And when I say "yes," that means we've published our results in the open medical literature explaining what's going on.

Q. Doctor, when you publish your results in the medical literature, is it sometimes illustrated with photographs?

A. I don't think I've ever published a paper without some kind of a figure or illustration, and usually it has many,

yes.

Q. So some of these slides that you are going to show us would have been parts of different publications?

A. Well, every one of them has so far. I mean, this one has and the next one, absolutely. Sure. Right.

Q. What's the next one, Doctor?

A. Okay. So the next slide I'm going to show you the lung of a rat from an -- from an experiment where the animal was exposed for a single hour. Because the first question was: Well, you see how complex the lung is, where do those fibers go when the animal inhales the dust? We know the answers now. But when we started, we certainly didn't know that.

So let me show you the answer to the question. So here now is the end of the airway where it opens into the gas exchange. And you are familiar with this now because we have been talking about these individual air spaces. And you know what the carpet looks like, it's those -- that smooth surface type 1 cells. And I'm going to focus the microscope right down here immediately after the single hour of exposure. Any asbestos fibers that we see on the carpet here must have been inhaled during that first hour.

So we have these chambers about six feet high, four feet wide. There is an asbestos generator at the top of the chamber. It makes it very dusty in the chamber. It's a high concentration of asbestos which the animals inhale for a

short time. They inhale for an hour, it could be two hours, it could be all day, it could be days, could be weeks. And I can take them out of the chamber, give them an overdose of anesthetic -- overdose means they don't wake up from that -- and then I choose the different times depending on the question I'm asking.

If the question is pretty straightforward, like where do the fibers go? I can learn that in an hour. If I want to know how long it takes for the scar tissue to develop it's going to take longer. If I want to know how long it takes to produce a lung cancer and what are the changes, it's going to take weeks and months of exposure. So those are the kinds of differences that are required to go through.

So let's focus on this spot right here in the lung. And this black hole right here is this black hole right here. So that means we are going to look at this surface right here. And here now on this surface we can see this is a 10 micron bar. So this fiber is about 10 microns long. There is kind of a long, curly fiber going up this way. There is some short, straight fibers. There is some curly ones here and some straight ones here.

So again, just like you saw sitting in the microscope, all the shapes and sizes that you see in this -- in this bundle of fibers now they are sitting on the air space surface on the carpet because this animal was inhaling

the dust. And it's like anybody, you don't get to see this in people, right? That's why we have to use the animals. You can't be exposing people to a toxic dust and then immediately get some lung tissue out. That's just not going to happen. That's why we use these animal models.

But since we know that this tissue is damaged in people exposed to asbestos, we then can follow the animal and say, Well, here is where the fibers landed, no wonder that was damaged in people. That's the kind of correlation you make between the animal model and people.

Q. So, Doctor, is this -- this was kind of like -- was it like a bifurcation between the airways?

A. Yeah. Right.

So for example, the air comes down here. And the air -- and whatever fibers in it can go down this hole. Or the air is going to -- I should say and some of the air goes up this way can go up here, or it can go this way, or there is a big bifurcation here so the air can go this way. So in other words, there are a series of splits and bifurcations.

Q. So a fork in the road?

A. A fork in the road. That's fine.

What we showed is that most of the asbestos actually collects at these bifurcation points. And that's what you are looking at when you see right here. That's why when you look at the lung of a person with asbestosis and lung cancer,

that's where those diseases tend to be the most pronounced, at those sites where they get the highest dose.

You have probably heard of dose response. The more --

Q. They did in opening.

A. The more asbestos you are exposed to, the more likely you are to get disease.

Now you are looking at a localized dose response. So here, this part of the lung right here gets a bigger dose than -- a bigger dose than it does farther away. So there is worse disease here than there is here. And there is worse disease here than there is here.

Q. That's because some of the fibers have gotten stuck on their way?

A. Yeah. Exactly right.

And so this localized dose response is something that we published -- we discovered and published in the open medical literature. And then other people started to look at that and say, Oh, look at that. And then, you know, repeated these experiments.

And then we actually went to the molecular level and started looking at which genes are produced at this site versus the site where there is less asbestos and no asbestos. And sure enough, there is a localized dose response at both the anatomic level and at the genetic level, okay?

So let's continue then on with understanding what this asbestos is doing and where it's going. Now, so here we can see the asbestos sitting on the carpet. But one of the more striking things that we saw was that some of the fibers are actually disappearing under the carpet. And I selected this picture to show you because you can see that happening here. You see, here are some fibers here but you can't see them here. They are actually under the carpet. And you can see them here in the carpet cells actually coming up over the top of the fiber. You can see the fibers here but you can't see them here.

So as I'm in the microscope room late at night and I'm looking at these fibers, I'm saying, Wait a second, I don't see these fibers here, where are they? So we had to do another whole series of experiments to prove that they were, in fact, under the carpet. And that's what our lungs do. We -- have we heard that we all have asbestos in our lungs?

Q. No, we haven't. Moff said he had some in his.

A. Okay. So we all have some asbestos in our lungs, a little bit that's accumulated over time from what's in the environment. Not enough to make us sick, but we all have some fibers. And some people it can be millions of fibers, but that's not a big deal, you can get a billion fibers into a thimble. Remember how small they are?

So where are those fibers? I ask rhetorically.

They are under the carpet. We have a compartment in all of our air spaces where we store things like that, a few fibers at a time under the carpet. Now, that includes fibers that can move from that space out to the pleura. And I'm going to explain how that happens because those are the fibers that cause mesothelioma. But first they have to get taken up, put into that space under the carpet and then transported to the pleura. So that's where we are going.

Q. Now, Doctor, you made this finding that these fibers are impacting here and getting taken under the carpet.

A. Right.

Q. And now then, was that the end of the story for where the fiber goes?

A. Well, no, because we want -- we want to know if they get to the pleura, so -- because that's the target site for mesothelioma.

Q. Okay. So what further studies did you do to determine what happens after the asbestos fibers goes under the carpet?

A. So understand, this is one place that this is going on out of millions around the lung. I'm just showing you one of them. And this is just one spot out of millions. And the same goes for the next picture that answers your question where the fiber is going. This is one spot out of millions. And we had to count thousands of them and prove to our peers what is actually happening.

Here you can see -- here you can see an air space, another air space. There is a little fiber bundle sitting on the carpet here. You can see some fibers here, but you can't see them here because of this process that I'm telling you about.

These epithelial cells, these carpet cells, respond very quickly to the presence of the fibers. They come up over the top of the fibers. And some of these type 1 cells are killed and damaged by the asbestos because these fibers are toxic.

Now, I think I told you there is a fiber bundle there. There is actually a fiber sitting here, but you can't see it. Maybe if you were close enough to that one you could probably see it. But there is a fiber completely covered here and all you can see is its electron shadow. But you can see these characters here that look like doughnuts. And this is what your red blood cells look like. There are about 5 microns from this side to this side. And they don't have a hole in the center like a doughnut, but they have a depression. So that's why they look like doughnuts. And you can see them lined up in small vessels as the blood runs through these small vessels.

Now, I say this is what your red blood cells look like, but this is the lung of a rat, okay? But this is exactly the same size and shape as yours and mine. And go

through the litany of animals that I did before, they all look and do the same thing.

Q. Blood cells are the same size?

A. Exactly. 5 microns across. This turned out to be evolutionarily the best size and shape to carry oxygen and carbon dioxide from the very first animals that did that to us today.

Q. So we maintain that 5 micron --

A. We main --

Q. -- red blood cell?

A. And shape, too. I mean, that's a very important shape for the cells being able to fit together as they are cramped into these small vessels called capillaries. So they are the best for the movement and the exchange of oxygen carbon dioxide.

Q. Is this the highest magnification we've seen yet?

A. No. Actually when you saw the macrophages you were.

Q. That was higher?

A. Yes.

Q. Okay.

A. Okay. So now we have these fibers moving -- look at this one here, you can see a little bit of it sticking up. But some of -- this fiber is actually moving into the blood flow. And we -- and other investigators have shown that asbestos gets into the blood flow in the lung. And if it gets into

the blood flow, it can go anywhere in the body, obviously.

But there is another more important flow for the movement of fibers to the pleura, and that's called lymph, L Y M P H. Lymph is a clear fluid that runs from head to toe in our bodies. Wherever there is blood flow, there is lymph flowing around it.

It has two major functions: The first major function of lymph is to control the pressure in our vessels. If you took at a blood vessel from the arm or leg or anywhere else and you cut across it, you would see a cuff around the outside of the blood vessel. There is lymph fluid running along there. And we can actually move fluids in and out of our blood vessels. And lymph is a part of that so we can help control the pressure. And sometimes you can actually feel swelling in your ankles and your wrists and other places where there is actually a backup of lymph fluid. That's what -- if your fingers feel all swollen, that is because there is lymph that has moved into that space.

Lymph is essential also for moving cells of the immune system. So sometimes you can actually feel that happening because we have these tissues called lymph nodes. Lymph nodes are small bundles of tissue that filter the lymph. Wherever lymph flows, it has to be filtered. And we have those nodes wherever lymph runs. So sometimes in our armpits or neck or groin you might feel discomfort because

you are fighting an infection and the -- and the immune cells that your body is sending to fight that infection are getting filtered out by the lymph nodes and you can feel that. You feel that it's some kind of discomfort.

Now, we have lymph flow in various, as I told you, in our bodies and in the lung. So let me show you what the lymph flow looks like in the lung. This is called a Netter diagram, N E T T E R. Dr. Netter has given us atlases of the human body in health and disease.

And here Dr. Netter is showing you these very fine vessels that reach the pleura. And what Dr. Netter is showing on the surface of the lung is this kind of reticular or network-like pattern of lymph, and this is a circulation. And here you can see these green blobs around the lung and those are lymph nodes in the chest cavity. And they are called thoracic lymph nodes because they are in the thorax in the chest cavity.

You have another set of lymph nodes in a lot of different places, but one set is in the peritoneal cavity that holds your stomach and your intestines. And that's important because -- I'm telling you about that because the second most likely place to get a mesothelioma is in the -- is in the peritoneal cavity. The peritoneal cavity, the covering of all your intestines, your stomach, your liver, those are all mesothelial cells, just like the outside cover

of the lung, mesothelial cells.

The most likely place to get mesothelioma is the lung. The second most likely place is the peritoneal cavity. Some of the investigators studied the lymph nodes around the lung and the lymph nodes in the peritoneal cavity. This is not my work, but they looked at people who were exposed to asbestos and they found increased accumulation of asbestos in the lymph nodes in both the chest and in the peritoneal cavity.

Now, that means that asbestos is flowing in the lymph. The only way asbestos can get into the lymph is by landing on the carpet, getting picked up by the carpet. About 20 percent of all the asbestos that lands on the carpet gets picked up by the cells and transported into the fluid flow that's the lymph.

In this space I was telling you about where we have -- where we store all these things, there is lymph. If I could, as I have, peel back the lung, and it's moist under that carpet, and that's from lymph. And so that's where a lot of asbestos goes. And now it can get into this lymph flow. And as Dr. Netter is showing you, this lymph flow can reach the pleura. And the target cells for mesothelioma are out here in the pleura.

Q. The parietal pleura or the visceral pleura?

A. So the visceral pleura is the pleura that covers the lung

and then the rib cage would be right here. And the rib cage is lined with mesothelial cells. And that's the parietal side. That's just the anatomic term for that side of the pleura. That's right.

Q. Same cells in both places?

A. Exactly. That's correct.

Now, I just wanted to digress for a second because we are going to start talking about cancer and how asbestos causes these target cells to become cancer cells. But I want to digress for a second because you can see here a bunch of macrophages. Here is the type 1 epithelium. Here is an air space down here. And there are a bunch of macrophages that have come in here to try to pick up these asbestos fibers. The problem is that these two macrophages are dead. This one is dying. It's got a fiber going right through it. Some of the fibers here, you can see they are sharing with one another. And this is a group of basically dead and dying macrophages.

Now, one of the things that we know that dead and dying macrophages do is that they send out what are called growth factors that cause other cells to divide. Now, a dividing cell, a cell that is making new cells, is more likely to become a cancer cell than a cell that's not dividing. So you don't want to have increased numbers of dividing cells if you can prevent that.

Q. How can you tell those macrophages are dying?

A. Well, just compare them to the way they are supposed to look, like in this guy back here, okay? The cell is ruffled and its membranes are complete. And this one has this character of showing it's in motion. And if you look at these characters, you can see this one has got a bunch of holes in it. Just look at them, they are a mess, right? They are tattered and they are just not normal looking macrophages. And this one is a little more normal than the others, but they are smooth surfaces which you never see in a normal macrophage. So that is how we know.

Q. And some macrophages are not able to defeat the asbestos?

A. Right.

And so what is going to happen is now -- they'll move. They can move towards the escalator. And other macrophages will come in and clean up the mess. And eventually they'll -- they do clear a lot of the fibers, but because of this, they can't clear them all because of this activity. And as I say, the damaged macrophages are playing a role in the disease process because they are causing other cells to divide.

Okay. So let's then -- unless you want to talk about any of these other things.

Q. That's another Netter drawing, isn't it?

A. All right. So we'll spend the rest of the time talking

about cancer. We have the asbestos at the target site. And we know that the mesothelial cells are covering the outside of the pleura.

Q. So what we have been talking about so far is the pathway towards the disease?

A. Pathway that the fibers take and the cells that they -- that are playing a part in getting those fibers to the target site.

Q. And these are the cells that they have interacted with along the way?

A. Yeah. Exactly. Sure.

Q. And they tend to harm those cells?

A. They do without a doubt, yeah. It's a very toxic agent, asbestos.

Okay. So this is another Netter diagram, and it is showing you -- I'm showing it to you because there is a smooth, normal pleura. That's what the pleura should look like. Shiny because it's moist, I told you about that. And that's what it should look like.

Now, compare that with the pleura of somebody with a mesothelioma. You see how dramatically thickened the pleura is? Both on the visceral pleura, as you point out, adjacent to the lung and the parietal pleura on the inside of the rib cage.

So this is an advanced case where the pleura --

where the mesothelioma has spread over the surface of the lung. It's even spread into the peritoneal cavity on the underside of the diagram, that big muscle that allows you to breathe. That's your breathing muscle.

Q. In order to meet the definition of a cancer, what has to happen with respect to invading other tissues?

A. Well, there are a couple of different questions there. Number one is what are the -- what are one of the hallmarks of a cancer? And that means if you are talking about invading other tissues, you are talking about a metastatic cancer. So that means that the cells are able to actually get free from or migrate from the original tumor and start another tumor. That's what that means. And that -- there are many cancers that do that.

Q. And in this particular drawing here, though, where we are showing the -- no, up in the middle, in the fissure -- what is that?

A. So this is the dividing line in the left lung between the upper lobe and the lower lobe. There is, as Mr. Herrick said, a fissure and it's lined by mesothelial cells. And here you can see the tumor is actually growing along that line and invading the lung. Not unusual for an advanced mesothelioma.

Q. Okay. So how does -- we've got this -- the asbestos at the site, and we've shown what the tumor looks like. I guess

you would say that's grossly --

A. Right. This is a gross anatomy, meaning you can see it with your naked eye; you don't need a microscope to see that. If you put these cells under the microscope, they have a particular characteristic which allows you to make a diagnosis as to what kind of cancer cells they are.

Q. What's the current thinking as to what's going on in the background that leads to this?

A. Okay. So how does the asbestos, as it reached the target cell, how did it cause this cancer to develop?

Q. Correct.

A. And so here I'll start by describing what's on this slide. And this is the cover of a proceedings of a meeting that I was at a few years ago. I gave a talk at this conference. And the conference was dedicated to understanding how fibers cause cancer. So there is the big word, carcino -- cancer -- genesis -- formation. So fibers causing cancer. And that was the focus of the meeting.

And I have been talking to you today about cells. I showed you that cells pick up fibers, and that is certainly part of the process. But you cannot talk about carcinogenesis unless you talk about the molecular aspects, and that means your genes. Molecular biology is the study of genes and genetics.

My last department that I was at before I retired as

a professor there was the Department of Molecular Biomedical Sciences. So biomedical science, the biology of medicine at the molecular level, molecular biomedical science. So there are Ph.D.s that can be had now in molecular biology. When I started there was no such thing, but now there are a number of scientists who are developing degrees in molecular biology. And they are studying genes and the way they function. And cancer is a genetic disease. All of the cancers are genetic diseases.

So I'm going to give you the simplest definition of cancer. Cancer is the loss of control of cell growth. I'm going to say that again and then I'm going to explain what that means. Cancer is the loss of control of cell growth. So humans have about 20,000 or so genes that make us what we are. And you can look around and you see various hair color, eye color, skin color. It's obvious what some of those genes do. But most of the genes, of those 20,000 or so genes, you don't get to see what they do. You don't see the genes in our liver that are making liver enzymes to digest their food and you don't see the genes that control our metabolic profiles. And we have genes that control other genes, okay?

So of those 20,000 or so genes, about 100 of them are called growth control genes. Now, I just told you that cancer is the loss of control of cell growth. We have about 100 growth controlled genes of the 20,000 or so that we have.

So cancer develops when there are mistakes, errors, sometimes mutations in a set of genes that controls cell growth.

So the next question is: How does asbestos or how do carcinogens -- you can answer in the broadest form -- how do carcinogens cause errors and mutations in genes that control cell growth? Well, there are a number of different ways, but we studied how asbestos does it. And it starts with what's going on in the cover of this.

Q. And describe for the jury what is going on on the cover.

A. So I told you that one of the ways that we study -- the way that we study these actions is by taking cells from animals or people, putting the cells in a dish. And take millions of them, you put them in a dish and give them the right nutrients, they will grow and divide and you can add the agents you are interested in.

And in fact, on the cover of this there are two cells. You see one over here and you can see the other one here. If you just look over here on the right for a second you can see them a lot more clearly. You can see this is one gene, this is one cell here and this is one cell over here. And notice the center circle in the cell. The center circle in the cell is called the nucleus. And you can see that some fibers were added. And you see the fibers around the outside of the nucleus, you can see kind of a long fiber there and some short fibers. Notice how all the fibers -- particularly

over here on this picture -- notice how all the fibers are excluded from the center circle, from the nucleus. Now, the reason they are excluded is because there is a membrane around it that protects what's in that nucleus. And all of our DNA, all of our genes, are in that nucleus. So we have a protected membrane that keeps foreign particles and agents out of the nucleus. I mean, that's the idea. That's what you want to happen.

Now, one of the things that we have known for a long time is that -- scientists have known -- is that when cells divide, they more likely become a cancer cell. I think I mentioned that to you earlier. You don't want cells dividing uncalled for and out of sequence in your body because they are more likely to become cancer cells.

So we asked in my laboratory, and with the -- working with adjacent laboratories and colleagues -- we asked what would happen if we added asbestos and other agents to the cells that were dividing? Here you can see if they are not dividing, the DNA is pretty well protected. But let's -- we can see then what happens if the cells divide. I'm glad you have this screen over here, so we can see what these pictures should actually look like.

Q. That's really washed out.

A. You can see there are three cells here, two cells on the outside are not dividing. The nucleus is intact. The DNA

has been stained blue so you can see what it actually looks like. And the cell in the center has received a signal to divide.

Now, you see this says normal cell division. So the idea, then, is to take -- when we make new cells, whether it's a skin cell or a lung cell, the idea is to make a perfect copy of all of the genes.

So let me tell you a little bit about your cell genes. I think -- could we take a break --

THE COURT: Sure.

THE WITNESS: -- possibly, Your Honor? I need to take a break.

THE COURT: You got it.

THE WITNESS: Thank you, Your Honor.

THE COURT: All right.

THE WITNESS: I'm not going to say why.

THE COURT: We'll start again in about 15 minutes, all right?

MR. HERRICK: Thank you, Your Honor.

(Thereupon, the jury retired from the courtroom.)

THE COURT: We'll start again in about ten minutes, 20 till.

(Thereupon, there was a brief recess.)

(Thereupon, the jury returned to the courtroom.)

THE COURT: Okay. Welcome back.

Mr. Herrick?

MR. HERRICK: Thank you, Judge.

Q. Dr. Brody, I believe when we left off we were talking about how you don't want to have your cells dividing because that's when they are more likely to have genetic errors and lead to cancer.

A. Right.

So let's talk about cell division for a minute. It's going on in all of us all the time. If I took a piece of your skin, I could show you under a microscope that about 10 percent of your cells are dividing and making new skin cells. That's a requirement for us to keep intact skin. Your lung and your liver, about 1 percent of those cells are dividing. You don't typically need to replace a lot of lung and liver cells. The mesothelial surfaces, one-half of 1 percent, so they have a very low rate of division. In injury, damage to the cells means you need to make new ones. So that's what's -- that's the point that I was making.

Now, that cell division is controlled by certain sets of genes. And I told you we have about a hundred of these growth control genes. No matter what kind of cells we have, no matter what kind of cell we are talking about, when we make new ones, we go through this process that's called cell division. And here are three cells, one, two and three. The two cells on the outside are not dividing. The

nucleus is intact. Again, you can see it better over here on this picture on the right. The cell in the center has received a signal to divide.

Now, if it were a cell sitting in a dish I could have added a growth hormone. If it were your skin, you had an injury, a cut or something and the cells around it need to divide and to fill in that space, whatever the situation is, if you have cell division, what happens is that all the DNA that's distributed in the nucleus condenses into these white threads that we call chromosomes. Chromosomes are bands of condensed DNA. And that's the cell -- I just found out I can draw on this thing. How about that?

So here you can see this cell is dividing, and all of the DNA has been condensed in these white threads called chromosomes. So chromosomes are bands of condensed DNA where all of the genes are distributed, all of the 20,000 or so genes are distributed. And we can see what those chromosomes look like in this next picture.

Let's see. This picture shows you that humans have 23 pairs of chromosomes. You've got one from your mother and one from your father. And those light and dark bands show where all of our genes are distributed. Here is another type. And I'm just pointing this out for you because the point is that all of our 20,000 or so genes must be on the correct chromosome and in the right place on that chromosome

to function. If they are not in the right place, they are not going to work.

And one of these genes I have an arrow on because the Human Genome Project showed us where it is in human chromosome 17, it's called p53. And p53 has many mechanisms of anticancer function. In fact, it's called a tumor suppressor gene. So this is a very important gene that we all have. And it's mutated in about 50 percent of all human cancers. So it's a very important protective gene that we have.

So let's see what happens when we put asbestos into the picture. First, let's finish the normal cell division. Here the cell, the chromosomes have collected, condensed. You can see here that they are going through a duplication. So if you had what's called faithful replication, with all the chromosomes and all the genes on the chromosomes in the right place, you get two what are called daughter cells. And you can see the daughter cells down here. And now we will have two cells just like the original and life goes on. And that is what is going on, as I say, in all of us all the time.

Now let's put asbestos into the picture. And here is one out of millions of cells in the experiment. Panel A, no asbestos. You can see half of the chromosomes go to one side, half to the other, and we'll have two daughter cells

and two new normal cells. But in panel B, this is from an experiment where we added Crocidolite asbestos. And you can see that this cell is about 40 microns across, and this fiber is about 30 microns, this one is 20 microns. Then there are some small fibers. And we put some arrowheads on here because some of this DNA is bound to the surface of the asbestos. That means that this DNA is not where it's supposed to be. And this results in this condition that you see up here called an aneuploidy, A N E U P L O I D Y. Aneuploidy means abnormal chromosome separation. I'm going to show you one more example of that caused by Chrysotile and in mesothelial cells.

So these kinds of experiments can be carried out in mesothelial cells, as well. And here you can see a normal mesothelial cell, half of the chromosomes no asbestos. Half of the chromosomes go to the one side; half to the other and you will have two daughter cells.

Now, here in this example the daughter cells have essentially formed. They haven't completely separated. You can see that the cells are still connected, but there is an asbestos fiber spanning the two cells and then there is some DNA bound to the surface of the fiber now again resulting in aneuploidy.

Now, these are not cancer cells, but the door has been opened. And the door has been opened because what I

just told you about the distribution of these various genes. Because if -- let's say that this part of chromosome 17 that has the DNA or the p53 gene, let's say that that is in this DNA that's bound to the surface of the Crocidolite fiber, that p53 gene is not going to function. Now, what does p53 do? P53, when it gets activated, stops the cell from dividing. And if the cell isn't dividing, it can't pass those mistakes on to the daughter cells which is a requirement for cancer. You have to keep passing these mistakes on to the daughter cells. P53 shuts it down. If there is a -- if there is damaged p53 or if p53 is not where it's supposed to be, it's not going to function.

Now we have another set of genes I'll tell you about. We have, as I said, about a hundred or so of these growth factor -- growth control genes. Another set of genes are called death pathway genes. So again, if there is DNA damage that, as you see here, the cell dies, and if the cell dies, again, it can't pass on those errors and pass them on to the daughter cells.

Q. So the cell dying is what you want to happen?
A. Exactly. And that's going on in all of us all the time.

There is a big word called apoptosis, A P O P T O S I S, program cell death. We have a series of genes that send the cell down a death pathway, you never hear from it again. You go out and get a sunburn, you cause aneuploidy,

the cells die by apoptosis and you never hear from them again. And that's a major protective device for us. Most of us are not going to get cancer. And no matter how much asbestos most of us are exposed to, we don't get mesothelioma. And the reason we don't get these cancers is because of these genetic defenses that we all have.

Now, for the person who has a cancer, what you know is that despite the genetic defenses that person had, there were some lapses or failures on the way or the -- there was enough asbestos for that person to produce the cancer.

So I have one more slide. And in that last slide I want to explain what's going on during that latency period. Because it's decades, and it's usually not clear to most people what's been going on during those decades, so let me explain.

So here is a -- the mesothelial cell surface. Again, it's more clear over here. You can see -- you think about the hundreds of millions of mesothelial cells sitting on the surface and then the artist has a couple of lightning bolts coming in here and he says DNA damage. That's what this says. DNA damage.

Now, as far as I know, lightning doesn't cause DNA damage. What we are talking about is a mesothelioma. So from the environment asbestos has reached the mesothelial surface. Asbestos is really the only known environmental

cause of mesothelioma. And in this case, we are talking about asbestos fibers reaching the mesothelial cell and causing DNA damage.

Now, you can see the cells dividing and we know that because we can see the chromosomes. The only time you can see the chromosomes is when the cell's dividing because the chromosomes have condensed. And one of the daughter cells is going off into the upper left-hand corner and dying because that's, the artist knows very well, that that's what happens to most DNA cells with DNA damage. And here you can see the DNA is clumped up. The surface of the cell is bubbling up. And there is even a macrophage coming up here to clean up the mess -- and as I say, that's going on in all of us all the time -- that protect us us from getting a cancer. But we are talking about a tumor. So therefore that means one of the daughter cells must have survived. And that's this daughter cell right here. And you can see it's dividing. You can see the chromosomes.

And then the author, the artist has given us a tumor, tumor genesis, tumor formation. And he's given us this cancer with the odd color and the dividing cells. And I'm going to tell you about that odd color in just a second, but I want you to understand what's going on in this space between the daughter cell and the developing tumor. This is the latency time. You've got to give me about 40 years in

there, okay? And I'm going to take about 30 seconds to tell you what's going on in those 40 years. So think about that mesothelial cell with a genetic error now sitting on the mesothelial surface. And that cell then will sit there with an error in p53 or any one of a number of other important genes that protect us. And that cell will sit there looking and acting like a normal mesothelial cell for months, but eventually, it has to divide. All of our cells have to divide at some point. And even though the mesothelial cells have a low background rate, it eventually has to divide: Two cells, four cells, eight cells, 16 cells, making a field of cells with that one error. Now, some of them may die. We have several different pathways to kill cells that have DNA damage. But in this case, they didn't all die because we've got a tumor.

So then you have one or more cells that, again, pick up a secondary, another asbestos fiber hits another cell. Now you have a cell with two genetic errors. And one error is not enough, two is not enough, three is not enough, four is probably not enough and five is not enough in most situations. Somewhere -- and it's different -- the reason I can't tell you exactly how many is because it's different for different people. And not only is the number different, but the combination of errors is different. There is about 20 different genes that I can tell you we expect to see, but the

combination is different for different people. So I can't tell you just which one you are going to see in a given tumor.

But now we are up to -- let's say we have two errors. And eventually the cell will sit there like that for months and eventually it has to divide: Two cells, four cells, eight cells, 16 cells, making that field -- some of them die. Immune system now can kick in.

The immune system is very good at recognizing potential tumor cells and killing them. We actually had a group of white blood cells called killer T cells. Lymphocytes. But that cell again can sit there with two or three errors looking and acting like a normal mesothelial cell for months. And then it has -- then it starts to divide again.

Okay. Now, I can stand here and do that for decades. Just think about that process going on for decades: Cells dividing, errors accumulating in different growth control genes, and decades later -- and our immune system and all of our genes that are designed to protect us, they are all working, they are all doing what they are supposed to do. But in the person who gets a cancer, decades after that initial -- those exposures that were required, a single cell with sufficient errors, sufficient number and combination for that person, grows out into this tumor. And that's why the

artist made this all the same color because he knows that we get clones of tumor cells growing out.

Now, you can have more than one clone, so you can have multiple places where an error -- where a cell with sufficient errors can grow out. But a single clone is sufficient to produce the disease. And whether you have single clones or multiple clones that grow together, nothing I said has changed, the concept is the same. And it's almost impossible to go back into a person and actually know whether it's from single or multiple clones, and it really doesn't matter. But the concept of how this occurs through the genetic errors takes decades because it takes so long for those errors to accumulate in sufficient number and culmination to bring that person to the clinic.

Q. Now, Doctor, of the slides that we've looked at in the ones that we've had, none of those have been of Mr. Sparkman's tissue?

A. That's correct. They have not.

Q. And in fact, I didn't ask you to look at Mr. Sparkman's tissue under the microscope?

A. You did not.

Q. I didn't give you his medical records to review or deposition testimony to review or anything like that?

A. That's correct.

Q. So how is this applicable, or is it applicable to Mr.

Sparkman?

A. Yeah. Well, I mean, this is the current understanding of how asbestos causes the genetic errors required to cause a cancer. It doesn't matter if it's Mr. Sparkman or anybody else. I mean, this is the general concept.

And actually, you remind me that I showed you this mechanism of DNA binding to the asbestos, but there is actually another probably equally as important -- I mean, we don't know just exactly which one is more or less important -- but it's called the generation of oxygen radicals. These are reactive oxygen species. These are high energy, short-lived chemical compounds that are generated by asbestos fibers. And we know that these reactive oxygen species damage DNA. That's the main way cigarette smoke causes lung cancer.

You have probably heard it's a good idea to take antioxidants. And I'm not saying to take antioxidants, what I'm saying is the concept of oxidants and reactive oxygen species is very clear in that they can be and are known to be powerful carcinogens, cancer causing agents.

Well, all of the asbestos varieties generate oxygen radicals. So asbestos can -- produces a double whammy, if you will. It not only binds DNA, but it also generates oxygen radicals. I didn't show you a picture of that because I can't take a picture of a chemical reaction. I showed you

the picture of the DNA binding, but I can't show you a picture of the reactions. But we've studied those in our laboratory and a number of other investigators have, as well, and they are very potent cancer causing agents.

Q. So with respect to Mr. Sparkman and his right pleural mesothelioma, these processes necessarily occurred in him?

A. To the best of science knowledge, science knowledge right now, I've just told you the two mechanisms that we understand take place in a person or experimental animal to cause a mesothelioma, that's correct.

Q. Can one fiber do that?

A. Well, no. One fiber is not sufficient to cause a mesothelioma. But you saw that individual fibers can bind DNA and can generate oxygen radicals. You saw the binding part. So the point is that every fiber can participate in the disease process. Now, we know that individual fibers are -- some of them are cleared and some of them get to the carpet and some of them get to the DNA. So the more individual fibers you are exposed to, the more likely you are to get the disease.

Q. Just a couple more questions, Doctor. Has science been able to determine a safe level of exposure below which people are not at risk for mesothelioma?

A. No. You are asking me about a threshold. In other words, is there a level below which we know will not cause

mesothelioma? And the answer is no, there is no level that's been shown to do that.

Now background, you know, if you include background in there, I would say the level that we all get is below the level that doesn't cause disease. But I mean, that's -- that's typically .000, one fiber per cubic centimeter, you need 1,000 of air to find one fiber. That is not a dose that produces disease. But above that background there is no safe levels that have been demonstrated.

Q. When you talk about all of us at a certain age that have asbestos in the lung, you are talking about what?

A. Well, I'm talking about over the decades of life we can accumulate millions of fibers, but that's not very much, and that's not enough to cause disease.

Q. And when one has a disease, the flip side of that, what is said about it? What caused that disease?

A. Well, if the disease is mesothelioma and there is an established asbestos exposure in that person's history, then you know the cause. And you know that whatever dose that person had was sufficient for that person. You can't say what is required for a given individual because, as I told you, no matter how much asbestos people are exposed to, typically they don't get mesothelioma. So that means in order to find out what happened to an individual, you need to -- you would have to go back and see what that person was

exposed to. And that's what caused their disease.

Q. And so when you -- when you talk about dose response, we are not talking about risk of disease, but dose response in somebody who already has the disease, does that factor together?

A. I'm sorry. Yeah. Risk is a theoretical likelihood. That's what epidemiologists do, they calculate a risk. How likely is it that a person is going to get disease? And then you can talk about dose response. The greater the dose, the more likely they are.

But once you have the disease -- and I'm not talking about risk because the risk turned out to be 100 percent for that person -- and so then you go back and see what they were exposed to and then you find out what caused their disease.

Q. And, Doctor, which type -- which type of asbestos fiber is most potent on a fiber per fiber basis in causing mesothelioma?

A. It appears to be Crocidolite over Amosite and Chrysotile. But we don't know by just how much. It does appear to be more potent on a fiber per fiber basis, meaning you would need -- so let's put it this way: If all you are exposed to is Crocidolite, you would need less asbestos than if all you were exposed to is Chrysotile. They all cause mesothelioma. Chrysotile, Amosite, Crocidolite by themselves can cause mesothelioma. But if all you are exposed to is Crocidolite,

you would need less of that fiber type than you would the others.

Q. And what's that understanding of the potency of Crocidolite based on, Doctor?

A. Well, it's largely epidemiology, the science of who gets sick from what. And there are more cases of mesothelioma when people are exposed to Crocidolite.

Q. All right. Doctor, you are going to charge me for your time in testifying today?

A. Sure.

Q. Tell me what your rate is.

A. $550 per hour.

MR. HERRICK: Thank you for coming to Charleston. I'll pass the witness.

CROSS-EXAMINATION

BY MR. MCDONALD:

Q. Dr. Brody, thanks, I appreciated your presentation.

A. Thank you.

Q. It's good to see you.

You've dedicated your life to learning more about asbestos-related disease; is that right?

A. Right.

Q. Yes. And what you showed us in here is some of the latest scientific information about that, right?

A. True.

Q. Here we are in 2015 and this is -- this is what we know now, right?

A. That's correct.

Q. Yeah. And a lot of what you showed us on the slides is actually animal cell division; things like that; is that right?

A. Well, I'm showing you what happens in people by using animals.

Q. Yeah.

A. But a lot of that was human tissue. I think I pointed that out.

Q. Yeah, you did. I just wanted to be clear.

When you showed the cells dividing and the errors, those were animal tissues?

A. Well, the ones I used, sure. But those same experiments have been done using human cells.

Q. And what you do with your mice is you expose them to massive doses of asbestos trying to get that response so you can study it; is that fair?

A. Not quite, okay? Because what we do is we give them a high concentration of dust --

Q. Okay.

A. -- for a short time.

Q. Sure.

A. So they actually get a small dose, but it's a sufficient

dose to produce lung injury and do what we need to do to follow the disease.
Q. And you will agree with me, of course, mesothelioma is a rare tumor?
A. It is. Sure.
Q. But again, it's a dose response disease. The higher the exposure, the higher the risk; the lower exposure, the lower the risks, right?
A. No question.
Q. And you mentioned Dr. Wagner a little bit. I didn't hear you mention Dr. Selikoff. Dr. Selikoff was a pioneer in asbestos medicine; is that right?
A. He sure was. He has invited me to give a talk in one of his conferences.
Q. Let's tell the jury a little bit. Dr. Selikoff, he started publishing papers in the mid-'60s?
A. Probably before that, in the '50s, but into the '60s, absolutely.
Q. And he was studying the insulators union, right?
A. That's right.
Q. And it was the men that put on steam pipe insulation and boiler insulation, and he was looking at their risk, right?
A. Exactly.
Q. Okay. And I believe he found that eventually, even though it's a rare tumor, 8 to 10 percent of those men

developed mesothelioma; is that fair?
A. The highest known percent in a population, that's correct, 10 percent.
So like I say, even the -- the population with the highest concentration that we know of in a workplace, 10 percent of the population got a mesothelioma. Huge numbers.
Q. Yes. And you mentioned that we viewed, even way back in the '30s, that asbestos caused disease, asbestosis, right?
A. That's right.
Q. Okay. And even back then -- for example, Dr. Dreesen suggested that there would be an appropriate level of exposure in factories even way back in the '30s; isn't that fair?
A. I think he did. I can't tell you what Dr. Dreesen said. Those aren't the kind of literature that I can give you the numbers, but I think you are right about that.
Q. And one thing that has confounded us is the long latency period of the disease; is that fair? So difficult to study populations, it takes so long to figure these things out that you are doing; is that fair?
A. I agree.
Q. Okay. And because of that, science has advanced so much, today's regulatory level is just a fraction of what was once considered appropriate in the workplace; is that fair?
A. I agree.

Q. Okay. And you will also agree, OSHA, EPA, they don't distinguish between the fiber types, right? They treat all asbestos as asbestos, right?

A. All of the asbestos fiber types cause all of the asbestos-type diseases. Sure.

Q. You talked about the amphiboles which would be more potent than the Chrysotile, right?

A. Causing mesothelioma, yes.

Q. Yes. And I think you will agree you find Amosite, which is an amphibole in the pipe covering insulation; is that right?

A. That's what I understand. That's right.

Q. Yes. Okay. And you did -- it's fascinating the way you talked about the way cancer starts. We are all exposed to carcinogens every day; isn't that fair?

A. All the time. That's why we have these genetic defenses that protect most of us.

Q. Exactly. I mean, you have to slow down and think about it for a second, I know you do every day, but the sun, for example, is a carcinogen, right?

A. Absolutely.

Q. Benzene is a carcinogen; is that fair?

A. Sure.

Q. And when I go put gasoline in my car, I get bathed in it; is that fair?

A. I hope you don't get bathed in it, but we certainly inhale it, sure.

Q. And there has even been some controversy about aflatoxin in peanut butter?

A. That's a powerful carcinogen.

Q. When I go home and make a peanut butter sandwich, I'm exposed to that, right?

A. All the time we are exposed. And our genetic defenses typically protect us.

Q. And that's what I was going to get to. Your body is amazing. These genetic changes happen, but your body has a way of destroying those cells almost all the time, right?

A. It's an excellent evolutionary principle. If every time we are faced with a carcinogen we died, you know, we wouldn't progress very far as a species.

Q. And I won't make you go back through all the defense mechanisms of the lung, but you will agree with me, if I breathe fibers, the fibers that I breathe in, the lung clears virtually all of them, right? Or very high percentages?

A. A high percentage, but not all of them.

Q. A very high percentage are cleared out?

A. That's true.

Q. And we were faced with a mesothelioma situation like Mr. Sparkman, it's impossible to go back and point and say, This fiber or that fiber caused the disease; is that fair?

A. Right. Whatever fibers he was exposed to in his history contributed to the development of the disease. That's right.

Q. And you will agree with me back in the day, back in the '50s and 60s, asbestos-containing products were very common, correct?

A. From what I understand, yes.

Q. Would you agree with me that over -- there were over 3,000 products that contained asbestos in the '60s; is that --

A. That's what I understand. Right.

Q. I'm going to flip through my notes here.

One thing. Let's be fair -- I want to be fair to the Sparkmans, okay? Smoking does not cause mesothelioma; is that right?

A. It does not. Cigarette smokers do not get mesothelioma and people who are exposed to asbestos and smoke don't have anymore mesothelioma than just asbestos exposure.

Q. When you do smoke on a cigarette, that slows down your defense mechanism?

A. Yeah. That has nothing to do with mesothelioma, like we just said.

Q. But you will agree with me it slows down the defense mechanisms?

A. Sure. And it's quite significant in the diagnosis of lung cancer.

Q. Let me flip through my notes here.

Of course, Dr. Brody, you've testified throughout the country?

A. Many times, yes.

Q. You still make about $200,000 a year testifying to juries like the jury here today?

A. Yes.

MR. MCDONALD: Okay. Let me just slow down and make sure I asked you everything I wanted to, Doctor. I think that's all my questions.

Thank you very much. It's good to see you.

THE WITNESS: You are welcome. Thank you.

MR. HERRICK: I don't have anything further. Thank you.

THE COURT: Okay, Dr. Brody, have a good trip home.

THE WITNESS: Thank you, Your Honor.

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I certify that the foregoing is a correct transcript from the record of proceedings in the above-titled matter.

Amy C. Diaz, RPR, CRR September 9, 2015

S/ Amy Diaz